

Title: Leukodystrophy Overview *GeneReview* Table 8

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Table 8. Disorders with Cerebellar Abnormalities on MRI

Feature		Inherited Disorder/Condition		Acquired Disorder / Condition
		Leukodystrophy	Not Leukodystrophy	
Middle cerebellar peduncle abnormalities		<ul style="list-style-type: none"> • ADLD ¹ • PBD, ZSS ² 	<ul style="list-style-type: none"> • FXTAS ³ 	
Hilus of the dentate involvement		<ul style="list-style-type: none"> • Alexander disease • Canavan disease • CTX ⁴ • Krabbe disease • MLC ⁵ • PBD, ZSS ² 	<ul style="list-style-type: none"> • 3-hydroxy-3-methylglutaryl-CoA lyase deficiency • Mitochondrial encephalopathies (e.g., those caused by mutations in <i>NUBPL</i>) 	<ul style="list-style-type: none"> • Langerhans cell histiocytosis (LCH)
Dentate nucleus involvement		<ul style="list-style-type: none"> • AGS ^{6,7} • Canavan disease • CRMCC ^{7,8} • L-2-hydroxyglutaric aciduria • PGBD ⁹ 	<ul style="list-style-type: none"> • 3-hydroxy-3-methylglutaryl-CoA lyase deficiency • Adenylosuccinase deficiency • Cockayne syndrome ⁷ • DRPLA ¹⁰ • Disorders of branched chain amino acids (BCAAS ¹¹) • Mitochondrial encephalopathies • Other amino acidopathies and organic acidurias • SSADH ¹² deficiency • Wilson disease 	<ul style="list-style-type: none"> • Langerhans cell histiocytosis (LCH)
Abnormal WM signal in cerebellum other than hilus of the dentate	Common	<ul style="list-style-type: none"> • 18q deletion syndrome • Alexander disease • CTX ⁴ • Krabbe disease • LBSL ¹³ starting from subcortical WM • Other peroxisomal disorders, starting from peridentate WM • PMD ¹⁴ • PMLD ¹⁵ • PGBD ⁹ 	<ul style="list-style-type: none"> • Disorders of branched chain amino acids (BCAAS ¹¹) 	<ul style="list-style-type: none"> • Langerhans cell histiocytosis (LCH) ¹⁷

Feature		Inherited Disorder/Condition		Acquired Disorder / Condition
		Leukodystrophy	Not Leukodystrophy	
Abnormal WM signal in cerebellum other than hilus of the dentate	Rare	<ul style="list-style-type: none"> • X-linked adrenoleukodystrophy 		
	More rare	<ul style="list-style-type: none"> • CACH/VWM ¹⁸ • MLC ⁵ • MLD ¹⁹ and its biochemical variants 		
Abnormalities within cerebellar cortex			<ul style="list-style-type: none"> • CDG ²⁰ • Dystroglycanopathies (cortical dysplasia) • GPR56-related disorders (cortical dysplasia) • Some SCA ²¹ 	
Cerebellar atrophy	Common	<ul style="list-style-type: none"> • HABC ²² • ODDD ²³ • Pol III-related leukodystrophies ²⁴ • Salla disease 	<ul style="list-style-type: none"> • Adenylosuccinase deficiency (atrophy / hypoplasia) • CDG ²⁰ • Cockayne syndrome & trichothiodystrophy • Dystroglycanopathies • Fatty acid hydroxylase-associated neurodegeneration (FAHN) • Glycine encephalopathy • LAMA2 MD ²⁵ • Mitochondrial encephalopathies • Molybdenum cofactor deficiency & isolated sulfite oxidase deficiency • NCL ²⁶ 	
	More rare	<ul style="list-style-type: none"> • CACH/VWM ¹⁷ • HDLS ²⁷ • L-2-hydroxyglutaric aciduria • MLC ⁵ • PGBD ⁹ • PMD ¹⁴ • PMLD ¹⁵ 	<ul style="list-style-type: none"> • DRPLA ³ • Galactosemia type I 	

Note: Disorders are ordered alphabetically.

1. AD adult-onset leukodystrophy

2. Peroxisome biogenesis disorders, Zellweger syndrome spectrum; includes neonatal adrenoleukodystrophy, infantile Refsum disease

3. Fragile X-associated tremor/ataxia syndrome
4. Cerebrotendinous xanthomatosis
5. Megalencephalic leukodystrophy w/subcortical cysts
6. Aicardi-Goutières syndrome
7. Calcium deposition
8. Cerebroretinal microangiopathy with calcifications and cysts; this disorder now appears to be distinct from Coats plus caused by mutations in CTC1, encoding conserved telomere maintenance component 1.
9. Polyglucosan body disease
10. Dentatorubropallidoluysian atrophy
11. Includes maple syrup urine disease (MSUD)
12. Succinic semialdehyde dehydrogenase
13. Leukoencephalopathy with brain stem and spinal cord involvement and lactate elevation
14. Pelizaeus Merzbacher disease
15. Pelizaeus Merzbacher like-disease
16. X-linked adrenoleukodystrophy
17. Confluent abnormalities in cerebellar WM; subcortical cerebellar ribbon of enhancement
18. Childhood ataxia with central nervous system hypomyelination / vanishing white matter
19. Metachromatic leukodystrophy
20. Congenital disorders of glycosylation; T₂ hyperintensity of the cortex as in [infantile neuroaxonal dystrophy](#), [Marinesco-Sjögren syndrome](#)
21. Spinocerebellar ataxia
22. Hypomyelination with atrophy of the basal ganglia and cerebellum
23. Oculodentodigital dysplasia
24. Includes hypomyelination, hypodontia, hypogonadotropic hypogonadism (4H syndrome); ataxia, delayed dentition, and hypomyelination (ADDH); tremor-ataxia with central hypomyelination (TACH); leukodystrophy with oligodontia (LO); and hypomyelination with cerebellar atrophy and hypoplasia of the corpus callosum (HCAHC).
25. LAMA2-related muscular dystrophy
26. Neuronal ceroid-lipofuscinoses
27. Hereditary diffuse leukoencephalopathy with spheroids. Also known as adult-onset leukodystrophy w/ neuroaxonal spheroids & pigmented glia; may include hereditary diffuse; pigmentary type of orthochromatic leukodystrophy w/pigmented glia (POLD).